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Abstracts

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Mesangiocapillary glomerulonephritis (MCGN) with "dense deposits" in the basement membranes of the kidney. *R. Vargas, K. Thomson, D. Wilson, J. S. Cameron, D. R. Turner, D. Gill, C. Chantler and C. S. Ogg. Departments of Pathology, Medicine and Paediatrics, Guy's Hospital, London.* Among 125 patients with mesangiocapillary glomerulonephritis, 19 showed continuous intramembranous "dense deposits". Most were children or young adults, many already with renal functional impairment, with arterial hypertension, a nephrotic syndrome and profuse, nonselective proteinuria. Some presented already in advanced chronic renal failure. Two patients had partial lipodystrophy. Twelve had a consistently low plasma concentration of C3; only three, however, had a low plasma C4 concentration initially, which rose and then remained normal. The C3NeF was positive in nine out of 13 cases and plasma C1q was normal in 8 out of 11 cases investigated. Eight out of 11 (6 of them with low plasma C3) showed C3 deposition by immunofluorescence in the glomeruli (linear in the glomerular basement membrane in 3 cases), as well as in Bowman's capsule and tubular basement membranes; IgG, IgA, C4 and C1q were negative in all, whereas IgM and fibrin were weakly positive in three and eight cases, respectively. Eight patients went into terminal renal failure over an average of 33 months and required hemodialysis or transplantation; so far two patients have died, one after renal transplantation; and one while receiving long-term hemodialysis. Two patients are alive with an allograft, and four are alive on regular dialysis treatment. Two patients showed rapidly progressive renal failure with extensive, occluding crescents on renal biopsy and were treated with prednisolone, azathioprine, dipyridamole and anticoagulant treatment. Nine others are alive on no specific treatment; only three of these 11 patients have a glomerular filtration rate (GFR) of less than 80 ml/min. MCGN with intramembranous "dense deposits" is an uncommon pattern of renal response to injury, which involves activation of the alternate pathway of the complement system, and has a poor short-term prognosis. The association with partial lipodystrophy and C3-splitting activity suggests a primary complement abnormality.

Immune-complex-mediated mouse malaria nephropathy. *C. R. P. George and J. S. Cameron. Department of Medicine, Guy's Hospital, London.* Adult male mice were inoculated intraperitoneally with 1×10 *Plasmodium berghei yoellii* parasites and cohorts of animals sacrificed at daily intervals. Animals of both TO and A_2G strains were used, since Petty, Steward and Soothill (*Clin Exp Immunol* 12:231, 1972) have shown them to produce antibody of high and low affinity, respectively. Study of renal histology showed the development of intraglomerular (predominantly mesangial) cell proliferation associated with granular mesangial deposition of immunoglobulins and C3 in all animals of both strains by day 8. In ensuing weeks immunoglobulin deposition also occurred in glomerular capillary basement membranes. The development and course of the renal disease was correlated with circulating antigen (malaria parasite) and antibody levels. Treatment with prednisolone, cyclophosphamide, azathioprine, dipyridamole, sulphinpyrazone or warfarin from the first day of infection failed to prevent or modify the renal disease, whereas elimination of the antigen with chloroquine did prevent development of the nephropathy. It is therefore concluded that *1*) mouse malaria nephropathy is a convenient and highly reproducible model of human immune-complex glomerulonephritis, and *2*) in the treatment of immune complex renal disease, elimination of the antigen will cure the disease, whereas corticosteroid, immunosuppressive and antithrombotic therapy fails to do this if antigenemia persists.

Observations on oliguria in the anesthetized dog. *Mary L. Forsling and Elisabeth Ullmann. Departments of Physiology, Middlesex Hospital Medical School and Medical College of St. Bartholomew's Hospital, London.* Oliguria during anesthesia and surgery is the result of several identifiable forms of stress, which activate several separate mechanisms including increased discharge of antidiuretic hormone (ADH) and increased secretion of catecholamines. Contrary to accepted opinion we found that, *irrespective* of the anesthetic used, a normal water diuresis can be induced in anesthetised dogs, provided stresses which elicit ADH release are carefully avoided. These are *a*) "pain", caused by operative trauma under *inadequate* anesthesia, *b*) hypotension and *c*) arterial hypoxia. Failure to induce a water diuresis, or subsequent oliguria was always related to one, or a combination, of these stresses. It proved much easier to induce and maintain a "water" diuresis if anesthesia was deep rather than light. Oliguria was more common when halothane was the anesthetic; but under halothane the dogs had a lower blood pressure, a greater tendency to systemic hypoxia and were more lightly anesthetised than dogs anesthetised by other methods. In contrast to several reports, we found that exogenous ADH (Pitressin) in doses adequate in the conscious animal, inhibited diuresis during anesthesia, provided it was a true "water" and not an "osmotic" diuresis. Pain and hypotension have long been known to provoke ADH release in conscious dog and man; hypoxia as a stimulus has so far received little attention, since it is rarely present in conscious animals, and because strict blood gas control during animal surgery is still uncommon. In our study direct assay of arginine vasopressin in plasma demonstrated that breathing 10% O_2 in N_2 for 15 min led to a large increase in plasma ADH and prolonged oliguria, together with a rise of blood pressure. In dogs pretreated with guanethidine, however, plasma ADH did not rise during hypoxia, an intriguing finding not yet explained. All the stresses mentioned are known to increase sympathetic nerve activity. The pattern of urine flow and concentration by itself did not enable us to distinguish clearly between the separate oliguric effects of ADH and catecholamines which may be additive in hypoxia. The precise role of the latter in stress oliguria remains to be assessed when arterial catecholamine concentration can be accurately measured, which may soon be possible.

Renal biopsy in acute renal failure. *J. D. Sraer, A. Kanfer, J. Marsac, F. Mignon, L. Morel-Maroger, G. Richet and J. Whitworth.*[1] *Service de Nèphrologie, Hôpital Tenon, Paris.* We have made a retrospective analysis of the clinical data and renal histological findings from 145 patients with acute renal failure

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who underwent renal biopsy. These patients formed 12% of all those with acute renal failure seen during the period 1966–1973. Indications for renal biopsy were *1)* oligoanuria persisting longer than three weeks; *2)* clinical signs suggestive of primary renal disease, vascular lesions or systemic disease; *3)* patients without an obvious cause for acute renal failure; and *4)* those with suspected drug toxicity. The histological findings are therefore more likely to be found in patients with acute renal failure considered *atypical* on clinical grounds. The lesions were predominantly tubular in 24% of patients, predominantly interstitial in 13%, glomerular in 29% and vascular in 32%. In three patients the appearances were unclassifiable. No glomeruli were obtained in only two patients (not discussed). Six patients suffered from clinically significant bleeding, and in one patient with microangiopathy, nephrectomy was necessary 30 days after the biopsy because of prolonged bleeding. This complication was almost confined to those patients with vascular lesions. We conclude that renal biopsy is a valuable investigation in selected patients with acute renal failure showing atypical features, aiding diagnosis, prognosis and treatment.

Effect of aluminium hydroxide therapy on calcium, phosphorus and aluminium metabolism in normal subjects. *J. Camm, V. A. Luck, J. B. Eastwood and H. E. de Wardener. Department of Medicine, Charing Cross Hospital Medical School, London.* Aluminium hydroxide gel is widely used as an antacid. In patients with renal failure, it is also used as a means of lowering the plasma phosphorus concentration. Earlier studies have shown that some of the ingested aluminium is absorbed. In eight patients with renal failure given 75 to 150 ml of aluminium hydroxide, there was a positive balance of 100 to 568 mg of aluminium/day. A further finding was that, although there was a consistent fall in plasma phosphorus, the change in phosphorus balance could be in either direction or not change at all. In the present study, aluminium hydroxide gel, 100 ml/day, was administered to five normal subjects. Observations were made on calcium, phosphorus and aluminium metabolism. There was a slight rise in plasma calcium but no change in calcium balance. The fasting plasma phosphorus concentration showed no change or a small rise. There was a large rise in fecal phosphorus but, because of a larger fall in urinary phosphorus, the balance of phosphorus tended to become more positive (or less negative) than that of the control period. The fall in urinary phosphorus, apparently occurring without a fall in fasting serum phosphorus, required explanation. Further studies of plasma phosphorus showed that during the daytime, when aluminium hydroxide was being taken, there was a fall in plasma phosphorus. This fall was more marked than during the control period. The amount of aluminium absorbed varied between 7 and 96 mg/day. This was considerably less than the amount of aluminium absorbed by the patients with chronic renal failure, $2P < 0.01$. This difference may be explained by the difference in phosphorus intake in the two groups.

Hemosiderosis due to parenteral administration of iron during regular hemodialysis: Treatment with desferrioxamine. *L. R. I. Baker, B. Brozovic, W. R. Cattell, J. M. McAlister and C. C. Nimmon. Department of Nephrology, St. Bartholomew's Hospital, London.* A 53-yr-old woman with chronic glomerulonephritis commenced regular hemodialysis (3 × 10 hr/week, using a Kiil dialyzer) in April, 1967. She received 5 ml of Ferrivenin i.v. thrice-weekly for the next 15 months, corresponding to approximately 19 g of elemental iron. Two pints of blood were transfused. Hepatosplenomegaly (liver, 12 cm; spleen, 6 cm) was noted in December, 1972. Liver biopsy revealed gross hemosiderosis (iron content, 2407 μg/100 g; upper limit of normal, 150 μg/100 g) and moderate periportal increase in reticulin. Liver architecture was preserved. Bone marrow iron stores were increased. After initial experiments with three different dose schedules, 2 g of deferoxamine was infused during the first three hours of each dialysis during the next 12 months. Iron removal during dialysis—which occurred predominantly during the first six hours of treatment—will be described. During the 12 months of treatment, serum iron and TIBC increased. A sharp decline in ^{59}Fe half-life occurred (before treatment, 7.0 yr; during treatment, 1.4 and 0.6 yr). The effect of treatment upon liver iron content and morphology will be described.

Atypical nondiabetic proteinuria and renal failure in patients with diabetes mellitus. *J. A. H. Wass, Victor Parsons, P. J. Watkins and F. E. Dische.* Six patients with proven diabetes mellitus, four insulin-dependent, two transiently so, presented with proteinuria and varieties of renal failure. Clinical presentation, absence of advanced retinopathy and renal biopsy provided evidence that diabetic patients are prone to similar glomerulopathies with and without the Kimmel-Stiel-Wilson lesions. The importance of renal biopsy diagnosis is emphasized as the prognosis and management of such patients may be entirely different from the conventional approach to patients with end-stage diabetic glomerular disease.